# MISSOURI NEWBORN SCREENING

## 2008 Annual Report



Missouri Department of Health and Senior Services

Governor Jay Nixon
Margaret T. Donnelly, Director

## Acknowledgments

The Missouri State Genetic Advisory Committee and its ancillary Newborn Screening Standing Committee, Sickle Cell Standing Committee, Cystic Fibrosis Standing Committee and Newborn Hearing Screening Standing Committee play a vital role in supporting the activities of the Missouri Department of Health and Senior Services Newborn Screening Program.

The expertise the committees provide is complemented by department staff who are motivated to help Missouri children receive the best care available when diagnosed with one of the serious medical conditions detectable through screening tests.


Missouri Department of Health and Senior Services
Division of Community and Public Health
Section for Healthy Families and Youth
Bureau of Genetics and Healthy Childhood
and
State Public Health Laboratory

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# What is Newborn Screening?



One of the great advances in preventive medicine has been newborn screening. Newborn screening is a public health program aimed at the early identification of conditions and the timely intervention by health care providers to eliminate or reduce associated mortality and morbidity. It is the goal that every newborn be screened for certain harmful or potentially fatal disorders that aren't otherwise apparent at birth.

Newborn screening tests ideally take place before a newborn leaves the hospital. Babies are screened to identify serious or life-threatening conditions before symptoms begin. Many of these disorders are metabolic in nature, which means they interfere with the body's ability to use nutrients to produce energy and maintain healthy tissue. Other types of disorders that may be detected through newborn screening include problems with hormones or blood disorders. These metabolic and other inherited disorders can interfere with an infant's normal physical and mental development in a variety of ways. In some instances they can even lead to death.

With a simple blood screen, doctors can often tell whether newborns have certain conditions that could eventually cause problems. The screening involves taking a few drops of blood by pricking the baby's heel and capturing the blood on a filter paper. The paper is sent to the newborn screening laboratory for screening, and results are sent back to the hospital of birth and the physician of record. If results are considered abnormal, the family will be contacted for further testing of the baby's blood.

Another newborn screening is a hearing screen. This is usually done while the newborn is sleeping and involves placing a tiny earphone in the baby's ear and measuring his or her response to sound. The baby experiences no discomfort from this procedure. Results from the hearing screening are provided immediately. The results tell the health care staff if further screening or an audiological assessment might be necessary.

The goal of Missouri's newborn screening program is for every newborn to be screened for certain harmful or potentially fatal disorders that aren't otherwise apparent at birth.

# Missouri Newborn Blood Spot Screening



In 2008, Missouri continued to expand the number of conditions for which infants born in the state are screened.

A pilot program for biotinidase deficiency screening was started by the State Public Health Laboratory's Newborn Screening Lab on Oct. 21, 2008. The pilot involved several discussions with the Newborn Screening Standing Committee, a subcommittee of the Missouri Genetic Advisory Committee; geneticists at Missouri's referral centers; program staff in the Bureau of Genetics and Healthy Childhood at the Missouri Department of Health and Senior Services; and state laboratory staff.

The pilot program was extended to Dec. 30, 2008, to provide more time to determine cutoff values for the condition and to determine decision schemes for reporting the screening results. Information was shared with the Newborn Screening Standing Committee before full implementation. Biotinidase deficiency screening was officially added to the newborn screening panel on Dec. 31, 2008.

During the pilot program, four babies were identified and ultimately confirmed for partial biotinidase deficiency and were placed on treatment.

Biotinidase deficiency is an inherited metabolic disorder of biotin (Vitamin B complex) recycling that leads to multiple carboxylase deficiencies. The genetic disorder is transmitted as an autosomal recessive disorder.

Infants with biotinidase deficiency appear normal at birth but develop one or more of the following symptoms after the first few weeks or months of life: ataxia, hypotonia, respiratory problems, seizures, hearing loss, alopecia, developmental delay, skin rash and metabolic acidosis that can result in coma and death.

Individuals with partial deficiency (a variant form) may also be at risk for development of any of the above symptoms, but symptoms are mild and occur only when the child is stressed, such as with a prolonged infection. Children may not be symptomatic until such time.

Biotinidase deficiency screening was officially added to Missouri's newborn screening panel on Dec. 31, 2008.

Missouri screens for both profound and partial biotinidase deficiency. Early detection is crucial. Treatment is simple, inexpensive and highly effective. All individuals with profound biotinidase deficiency, even those who have some residual enzymatic activity, should have lifelong treatment with biotin therapy. This involves taking varying amounts of the vitamin biotin, which should be done in consultation with a pediatric metabolic specialist.

Estimated prevalence of biotinidase deficiency for profound deficiency (absent enzyme) is one in 112,000 births in Missouri. Estimated prevalence for profound and partial biotinidase deficiency together is one in 60,000 births in Missouri.

The condition occurs in all ethnic groups.

## Next Steps

Missouri has met the goal of screening for all 29 core conditions recommended by the American College of Medical Genetics and the March of Dimes has with the addition of the biotinidase deficiency screening. When considering secondary conditions, a total of 67 disorders can be detected through newborn screening.

Many changes have been instituted since newborn screening became a standard practice more than 40 years ago. Missouri and other states mandate newborn screening of all infants born within their border. Newborns typically appear normal at birth with no sign of any disorder until a developmental disability or death occurs. Upon detection of a condition, specialists formulate a plan of medical management that allows most affected newborns to develop normally. Newborn screening is a model for public health-based population genetic screening. It is recognized nationally and internationally as an essential public health program that provides for the best outcomes for the nation's newborn population.

As more information about various genetic, endocrine and metabolic conditions is discovered on the national and international level, the expansion of newborn screening will continue to evolve.

## Missouri Newborn Screening Disorders

Newborn screening disorders tested and reported in Missouri are:

- Biotinidase deficiency (BIO)
- Classical galactosemia (GALT)
- Congenital adrenal hyperplasia (CAH)
- Congenital primary hypothyroidism (CH)
- Cystic fibrosis (CF)

- Amino Acid Disorders
  - Arginemia (ARG, arginase deficiency)
  - Argininosuccinate acidemia (ASA, argininosuccinase)
  - Citrullinemia type I (CIT-I, argininosuccinate synthetase)
  - Citrullinemia type II (CIT-II, citrin deficiency)
  - Defects of biopterin cofactor biosynthesis (BIOPT-BS)
  - Defects of biopterin cofactor regeneration (BIOPT-RG)
  - Homocystinuria (HCY, cystathionine beta synthase)
  - Hyperphenylalaninemia (H-PHE)
  - Hypermethioninemia (MET)
  - Maple syrup urine disease (MSUD, branched-chain ketoacid dehydrogenase)
  - Phenylketonuria (PKU, phenylalanine hydroxylase)
  - Tyrosinemia type I (TYR-1, fumarylacetoacetate hydrolase)*
  - Tyrosinemia type II (TYR-II, tyrosine aminotransferase)
  - Tyrosinemia type III (TYR-III, hydroxyphenylpyruvate dioxygenase)

- Fatty Acid Disorders
  - Carnitine acylcarnitine translocase deficiency (CACT)
  - Carnitine uptake defect (CUD, carnitine transport defect)*
  - Carnitine palmitoyl transferase deficiency I (CPT-1a)
  - Carnitine palmitoyl transferase deficiency II (CPT-II)
  - Dienoyl-CoA reductase deficiency (DE-RED)
  - Glutaric acidemia type II (GA-II, multiple acyl-CoA dehydrogenase deficiency)
  - Long-chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
  - Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
  - Medium-chain ketoacyl-CoA thiolase deficiency (MCKAT)
  - Medium/Short chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (M/SCHAD)
  - Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
  - Trifunctional protein deficiency (TFP)
  - Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

- Organic Acid Disorders
  - 2-Methyl-3-hydroxybutyric aciduria (2M3HBA)
  - 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG, SBCAD)
  - 3-Hydroxy 3-methylglutaric aciduria (HMG, 3-Hydrox 3-methylglutaryl-CoA lyase)
  - 3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)
  - 3-Methylglutaconic aciduria (3MGA, Type I hydratase deficiency)

- Beta ketothiolase (BKT, mitochondrial acetoacetyl-CoA thiolase, short-chain ketoacyl thiolase)
- Glutaric acidemia type I (GA-1, glutaryl-CoA dehydrogenase)
- Isobutyryl-CoA dehydrogenase deficiency (IBG)
- Isovaleric acidemia (IVA, Isovaleryl-CoA dehydrogenase)
- Malonic acidemia (MAL, malonyl-CoA decarboxylase)
- Methylmalonic acidemia (CBL A,B; vitamin B12 disorders)

• Organic Acid Disorders (continued)
- Methylmalonic acidemia (CBL C,D)
- Methylmalonic acidemia (MUT, methylmalonyl-CoA mutase)
- Multiple carboxylase deficiency (MCD, holocarboxylase synthetase)
- Propionic acidemia (PROP, propionyl-CoA carboxylase)

• Hemoglobinopathies
- Sickle cell disease (Hb S/S)
- Sickle hemoglobin-C disease (Hb S/C)
- Sickle beta zero thalassemia disease
- Sickle beta plus thalassemia disease
- Sickle hemoglobin-D disease
- Sickle hemoglobin-E disease
- Sickle hemoglobin-O-Arab disease
- Sickle hemoglobin Lepore Boston disease
- Sickle HPFH disorder
- Sickle “Unidentified”
- Hemoglobin-C beta zero thalassemia disease
- Hemoglobin-C beta plus thalassemia disease
- Hemoglobin-E beta zero thalassemia disease
- Hemoglobin-E beta plus thalassemia disease
- Hemoglobin-H disease
- Homozygous beta zero thalassemia disease
- Homozygous-C disease
- Homozygous-E disorder
- Double heterozygous beta thalassemia disease

• Others
- Hearing

* There is a lower probability of detection of this disorder during the immediate newborn period.

The Missouri Newborn Screening Laboratory’s goal is to identify infants at risk and in need of diagnostic testing for the above disorders. A normal screening result does NOT rule out the possibility of an underlying metabolic/genetic disease.

# Screening Spotlight: Hemoglobinopathy



The primary purpose of newborn hemoglobinopathy screening is to identify infants with sickle cell disease for whom early intervention has been shown to reduce morbidity and mortality.

Prophylactic antibiotic treatment, parent counseling and continual observation of the child's health greatly reduces deaths from bacteremia, pneumonia and meningitis in infants with sickle cell disease and can considerably improve their health outcomes.

Sickle cell disease refers to a group of genetic disorders characterized by the predominance of hemoglobin S (Hb S). The Hb S causes normal round blood cells to change to a crescent or sickle shape. These sickle-shaped cells clog the bloodstream causing obstructions that result in serious medical problems, including anemia, painful episodes, stroke, tissue damage and organ failure. Infants with sickle cell disease also have compromised immune systems making them much more vulnerable to bacterial infections.

Other abnormal hemoglobinopathies and most abnormal hemoglobin trait conditions can be detected through newborn screening; however, it is not possible to identify beta thalassemia trait on newborn screening samples.

## Incidence

Sickle cell disease occurs most commonly in people of African descent, but can also affect people of Middle Eastern, Indian, South and Central American, Caribbean, and Mediterranean descent. One in every 400 African-American newborns has some form of sickle cell disease, and approximately one in 12 African-Americans has sickle cell trait.

## Inheritance

Sickle cell diseases are inherited in an autosomal recessive pattern, meaning that for a hemoglobinopathy disease condition to exist, an abnormal hemoglobin or thalassemia typically must be inherited from both parents. Sickle cell anemia (SS) occurs when one gene for Hb S is inherited from both parents. Other sickling disorders occur when a gene for Hb S is inherited from one parent and another abnormal gene, such as C, E, or beta thalassemia, is inherited from the other parent.

## Variant Forms

There are hundreds of different hemoglobin types, and as a result, many different forms of hemoglobinopathies exist. Sickle cell anemia (Hb SS) is the most common type of sickle cell disease. There are other hemoglobin genes (C, E, beta thalassemia) which, in combination with the gene for sickle hemoglobin, can result in different forms of sickle cell disease (Hb SC, Hb SE, Hb S/beta thalassemia).

## Methodology

Missouri started universal screening for sickle cell disease in 1989. Each year approximately 40 infants are identified with a form of sickle cell disease. The Newborn Screening Lab uses a two-tiered screening system whereby all specimens are tested using Isoelectric Focusing (IEF), which is electrophoresis in a pH gradient. Any samples obtaining abnormal or questionable results are re-assayed using the next level of testing, which is High Performance Liquid Chromatography (HPLC). These two methodologies are highly complementary in sensitivity and specificity, detecting not only disease conditions but also infants who are trait carriers.

**Prevalence (Missouri):**
1:400 (Sickle cell disease in African-Americans)
1:3000 (Sickle cell disease in General Population)
1:1700 (Hemoglobinopathies in General Population)

**Analytes Measured:**
Hemoglobin fractions
Fetal (F), Adult (A), Sickle (S), C-Hemoglobin (C), E-Hemoglobin (E), D-Hemoglobin (D). O-Arab (O), Lepore Boston, Bart's, and Unidentified Hemoglobins

**Reporting Ranges:**
FA = Normal
FS = Homozygous S, Sickle thalassemia, or Sickle HPFH (Hereditary Persistence of Fetal Hemoglobin)
FSC = Sickle Hemoglobin-C disease
FSA = Sickle beta plus thalassemia
FSD = Sickle Hemoglobin-D disease
FSE = Sickle Hemoglobin-E disease
FSO = Sickle-O-Arab disease
FSLepore = Sickle Lepore Boston disease
FSX = Hemoglobin S with unidentified hemoglobin
FC = Homozygous C or C – thalassemia
FCA = Hemoglobin-C beta plus thalassemia
FE = Homozygous E or E – thalassemia
FEA = Hemoglobin-E beta plus thalassemia
F only = Possible homozygous beta thalassemia
High Bart's level = Hemoglobin H disease

**Feeding Effect:** None

**Timing Effect:** None (unless transfusion is needed)

Note: Sample collection after a transfusion with red blood cells invalidates hemoglobin test results for a minimum of 90 days post transfusion. It is recommended that a sample is collected prior to a transfusion, if at all possible. If a baby has been transfused prior to sample collection, it should be noted on the collection form.

**Confirmation:** Whole blood repeat samples collected from the infant and both parents within two weeks. The Missouri State Lab can provide blood collection kits and no-cost testing.

**Treatment:** Prophylactic antibiotics

**Screening Practice Considerations**

- The newborn screen should detect most abnormal hemoglobin variants; however, it is not possible to identify beta thalassemia trait on newborn screening samples.
- The hemoglobinopathy newborn screen is not affected by age at collection.
- Blood transfusions may cause false negative results, so a newborn screening specimen should always be obtained prior to a transfusion.
- The screening test is not diagnostic, and all results positive for hemoglobinopathy conditions should be confirmed. Early diagnosis of sickle cell disease is critical so children who have the disease can receive proper treatment.
- Hemoglobinopathies are complex disorders. Consultation should be made with a Hemoglobinopathy Resource Center for additional information concerning the results and appropriate follow-up and treatment.

## Confirmation and Treatment

Every infant with a presumptive positive hemoglobinopathy screening result must have confirmatory testing done in a timely manner.

When a newborn screen indicates sickle cell disease, a definitive diagnosis should be established by the primary physician, or the patient should be referred to a pediatric hematologist. All abnormal newborn screening results indicating a sickle cell disorder require appropriate confirmatory testing with the results of the diagnosis reported back to the Missouri Department of Health and Senior Services on the follow-up forms provided.

Several testing methods are recommended for diagnosis of sickling disorders and other hemoglobinopathies. Hemoglobin electrophoresis – including both cellulose acetate and citrate agars, isoelectric focusing, and high performance liquid chromatography – are considered proven, reliable and accurate methods for defining hemoglobin phenotypes.

Clinical guidelines established by the National Institutes of Health for management of sickle cell disease recommend that penicillin prophylaxis should begin by 2 months of age for infants with suspected sickle cell anemia, whether or not the definitive diagnosis has been established. It is also recommended that antibiotic treatment should continue until at least 5 years of age.

Any sign of illness in an infant with sickle cell disease is a potential medical emergency.

# The Newborn Screening Process

## 1: TESTING

- The baby's heel is pricked and a few drops of blood are collected on a filter paper 24 to 48 hours after birth.


- The dried blood spot specimen is shipped to the State Public Health Laboratory.
- Specimen is tested for multiple conditions.

## 2: FOLLOW-UP

- Positive screen results are reported by phone/ fax/letter from lab and follow-up staff to baby's physician. Results are also sent to the appropriate Genetic Tertiary Center in Missouri for follow-up.

- Specimen screening results are entered into data system.
- Baby's physician or health care provider contacts baby's parents.

- Parents bring baby back in for evaluation and more testing at the genetic center.

## 3: DIAGNOSIS/ INTERVENTION

- Depending on the screen result and the condition screened, repeat or confirmatory testing occurs at the genetic center.

- Parent education for signs/symptoms to watch for is conducted.

- Baby's physician consults with the specialist appropriate to the condition.

## 4: TREATMENT & MANAGEMENT

- Once diagnosis is made, treatment begins. For some life-threatening conditions, treatment may occur prior to diagnosis - on the recommendation of a specialist.

- Parents receive treatment guidelines/ education. Team support services as appropriate, include:
  - Metabolic dietitian monitoring and consultation
  - Ongoing blood monitoring
  - Referral to early intervention services
  - Pulmonary/CF services
  - Pediatriac endocrine monitoring
  - Pediatric hematology monitoring
  - Genetic counseling and consideration of family testing
  - Other allied health services as needed

# Missouri Newborn Hearing Screening



The Centers for Disease Control and Prevention (CDC) recommends that all infants be screened for hearing loss by one month of age. Infants who screen positive for hearing loss should receive an audiologic evaluation by three months of age, and infants with confirmed hearing loss should receive early medical and intervention services by 6 months of age.

Provisional 2008 hearing screening data for Missouri show:

- 80,861 live births
- 79,033 (97.7 percent) infants screened by 1 month of age
- 1,649 (2.0 percent) infants screened after 1 month of age
- 1,304 infants failed their final screening or missed a screening
- 425 (32.5 percent) infants received audiologic evaluation by 3 months of age
- 147 infants diagnosed with a permanent hearing loss
- 20 (13.6 percent) infants received early intervention services by 6 months of age

Note: This data was obtained on August 6, 2009, and is subject to change because the process of collecting and analyzing the data is ongoing. It is anticipated that a final review with the Missouri Department of Elementary and Secondary Education (DESE) will result in a far greater number of children known to have received intervention services prior to 6 months of age.

In an effort to reduce loss to follow-up after failure to pass the newborn hearing screening, the Missouri Newborn Hearing Screening Program (MNHSP) planned a pilot project with three Missouri hospitals that began July 1, 2008. Two of the three hospitals remained with the project for the entire year and have continued to participate.

The pilot hospitals agreed to use a script to inform parents about non-passing results and to explain the importance of returning for another screening or for an audiologic evaluation. Additionally, the hospitals made follow-up appointments for these families. The MNHSP made reminder phone calls to the families prior to the appointment date and sent a letter of notification to each baby's physician.

Provisional results are heartening and show that one hospital reduced its lost to follow-up after failure to pass the newborn hearing screening rate by 30 percent, and the other hosptial reduced its rate by 28 percent. At this time, the MNHSP is recruiting additional hospitals to join the project.

Nearly 98 percent of infants born in Missouri in 2008 were screened for hearing loss by one month of age.

In 2008, the MNHSP evaluated data from the MOHear Service Coordination joint DHSS/DESE project that took place in the Kansas City region. The specialized service coordinator visited 13 families in their homes in conjunction with a First Steps service coordinator and acted as a resource person by way of phone calls and emails for five additional families.

Infants with confirmed hearing loss should receive early medical and intervention services by 6 months of age.

In satisfaction surveys, families and First Steps service coordinators commended the program, which provided unbiased information about communication options to families of infants recently diagnosed with permanent hearing loss. At this time, the MNHSP is exploring opportunities for statewide expansion of the program.

The MNHSP also distributed sample copies of a booklet developed by the National Center for Hearing Assessment and Management (NCHAM) called "Communicating With Your Child." The booklet is designed for families of infants and children recently diagnosed with permanent hearing loss. The NCHAM worked with a group of consumers, EHDI program coordinators, and family advocates to develop material that is brief, but provides essential information and is at an appropriate reading level. NCHAM worked with the MNHSP to develop a Missouri-specific "Find Out More" page. These inserts were included in samples given to Missouri pediatric audiologists and First Steps Single Point of Entry (SPOE) Directors. Following tremendous positive feedback to these booklets, the MNHSP sent booklets to every group that requested them after the initial review.

To aid hospital newborn hearing screening programs in the training of screeners, the MNHSP sent every birth hospital and birth clinic an NCHAM-produced DVD titled: "Newborn Hearing Screening Training Curriculum (NHSTC)." The DVD package contained two discs. The first disc covered all aspects of the newborn hearing screening and follow-up process. Each section contained learning objectives and a test at the end that could be used to fulfill hospital competencies. The second disc contained test questions and answers, scripts and frequently asked questions for screeners to use with parents in Spanish and English and related Web sites.

In addition, the MNHSP included one CDC 1-3-6 "Just in Time" poster, two laminated "Top Ten Things to Remember When Filling out the Hearing Screening Result Form" reminders, and two laminated pictorial "Newborn Hearing Screening Process" flow charts for the benefit of screeners and those who complete the result forms. Hospitals found these materials useful in assisting their newborn hearing screening programs to improve standards of care to the babies and families through efficient, effective and comprehensive screening practices.

## *Next Steps*

The MNHSP will continue to decrease loss to follow-up after failure to pass the newborn hearing screening rates by expanding the pilot program into other hospitals. To date, three more hospitals agreed to begin the project in September 2009. The MNSHP continues to recruit and welcomes inquiries from interested hospitals.

To further ensure families return for a rescreen or audiologic evaluation following their newborn's failure to pass the initial newborn hearing screening, the MNHSP will create a brochure for families titled, "Your Baby Needs Another Hearing Test." The informational brochure will emphasize the importance of determining hearing status in order to ensure the timely development of communication skills. The brochure will be available to all hospital and birth clinic screening programs.

# Newborn Screening Contact Information

## Telephone Contacts:

| | |
|---|---|
| Newborn Screening Laboratory main number | 573-751-2662 |
| Order newborn screening specimen forms; person | 573-751-3334 |
| Order newborn screening specimen forms; automated attendant | 573-522-4991, Ext. 3226 |
| Genetics and Healthy Childhood, for follow-up information | 1-800-877-6246 |

## Web Addresses:

Newborn Screening Laboratory – http://www.dhss.mo.gov/Lab/Newborn/index.html

Newborn Screening Program – http://www.dhss.mo.gov/Genetic/index.html

Newborn Hearing Screening Program – http://www.dhss.mo.gov/NewbornHearing/

## Appendix 1: Disorders Confirmed for 2008 and Projected Incidence Rates

| DISORDER | DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE | PROJECTED INCIDENCE RATE |
|---|---|---|
| **Amino Acid Disorders** | **10** | **1/8,000*** |
| Arginemia | | |
| Argininosuccinate acidemia | | |
| Citrullinemia type I | 2 | |
| Citrullinemia type II | | |
| Defects of biopterin cofactor biosynthesis | | |
| Defects of biopterin cofactor regeneration | | |
| Homocystinuria | | |
| Hypermethioninemia | | |
| Hyperphenylalaninemia | 3 | |
| Maple syrup urine disease | | |
| Maternal PKU | | |
| Phenylketonuria (PKU) | 5 | 1/15,000 |
| Tyrosinemia type I | | |
| Tyrosinemia type II | | |
| Tyrosinemia type III | | |
| **Biotinidase Deficiency**** | **0** | **1/112,000** |
| **Classical galactosemia (GALT)** | **0** | **1/50,000** |
| **Congenital adrenal hyperplasia (CAH)** | **5** | **1/13,000** |
| **Congenital primary hypothyroidism (CH)** | **35** | **1/3,000** |
| **Cystic fibrosis (CF)** | **25** | **1/4,000** |
| **Fatty Acid Oxidation Disorders** | **21** | **1/10,000*** |
| Carnitine acylcarnitine translocase deficiency | | |
| Carnitine uptake defect | | |
| Carnitine palmitoyl transferase deficiency I | | |
| Carnitine palmitoyl transferase deficiency II | | |
| Dienoyl-CoA reductase deficiency | | |
| Glutaric academia type II | | |
| Long-chain hydroxyacyl-CoA dehydrogenase deficiency | 1 | |
| Medium-chain acyl-CoA dehydrogenase deficiency | 12 | |
| Medium-chain ketoacyl-CoA thiolase deficiency | | |
| Medium/Short chain L-3 hydroxy acyl-CoA dehydrogenase deficiency | | |
| Short-chain acyl-CoA dehydrogenase deficiency | 4 | |
| Trifunctional protein deficiency | | |
| Very-long chain acyl-CoA dehydrogenase deficiency | 3 | |
| Unknown fatty acid oxidation disorder | **1** | |

| DISORDER | DIAGNOSIS CONFIRMED AS POSITIVE AND UNDER MEDICAL CARE | PROJECTED INCIDENCE RATE |
|---|---|---|
| **Organic Acid Disorders** | **10** | **1/25,000*** |
| 2-Methyl-3-hydroxybutyric aciduria | | |
| 2-Methylbutyryl-CoA dehydrogenase deficiency | 1 | |
| 3-Hydroxy 3-methylglutaric aciduria | | |
| 3-Methylcrotonyl-CoA carboxylase deficiency | 3 | |
| 3-Methylglutaconic aciduria | | |
| Beta ketothiolase | | |
| Glutaric acidemia, type I | 2 | |
| Isobutyryl-CoA dehydrogenase deficiency | 1 | |
| Isovaleric acidemia | 1 | |
| Malonic acidemia | | |
| Methylmalonic acidemia (CBL A,B; vitamin B12 disorders) | | |
| Methylmalonic acidemia (CBL, C,D) | | |
| Methylmalonic acidemia (MUT, methylmalonyl-CoA mutase) | | |
| Multiple carboxylase deficiency | | |
| Propionic acidemia | 1 | |
| Unknown organic acid disorder | 1 | |
| **Hemoglobinopathies** | **39** | **1/1,700*** |
| Sickle cell anemia disease (Hb S/S) | 20 | **1/3,000** Total population; **1/400** African-American population |
| Sickle hemoglobin-C disease (FSC) | 11 | |
| Sickle beta zero thalassemia disease | 2 | |
| Sickle beta plus thalassemia disease (FSA) | | |
| Sickle hemoglobin-D disease | | |
| Sickle hemoglobin-E disease | | |
| Sickle hemoglobin-O-Arab disease | | |
| Sickle hemoglobin Lepore Boston disease | | |
| Sickle HPFH disorder | | |
| Sickle “Unidentified” | 2 | |
| Homozygous-C disease (FC) | 3 | |
| Hemoglobin-C beta zero thalassemia disease | 1 | |
| Hemoglobin-C beta plus thalassemia disease | | |
| Homozygous-E disorder (FE) | | |
| Hemoglobin-E beta zero thalassemia disease | | |
| Hemoglobin-E beta plus thalassemia disease | | |
| Homozygous beta zero thalassemia disease | | |
| Double heterozygous beta thalassemia disease | | |
| Hemoglobin-H disease (Highly Elevated Barts) | | |
| Other (FCE) | | |

* Combined incidence of all disorders in this category.

** Officially added to the newborn screening panel on December 31, 2008.

## Appendix 2: Newborn Screening Laboratory Report – Specimens Received 2008

| | Number Babies Tested | Specimens Received | | | Total Infant Specimens |
|---|---|---|---|---|---|
| | | Initial | Repeat | Unsatisfactory | |
| **Jan** | 6946 | 6946 | 715 | 280 | 7941 |
| **Feb** | 6353 | 6353 | 582 | 208 | 7143 |
| **Mar** | 6425 | 6425 | 647 | 209 | 7281 |
| **Apr** | 6990 | 6990 | 663 | 145 | 7798 |
| **May** | 6498 | 6498 | 584 | 146 | 7228 |
| **Jun** | 6609 | 6609 | 592 | 92 | 7293 |
| **Jul** | 7571 | 7571 | 577 | 108 | 8256 |
| **Aug** | 6801 | 6801 | 624 | 100 | 7525 |
| **Sep** | 7550 | 7550 | 743 | 132 | 8425 |
| **Oct** | 6716 | 6716 | 743 | 148 | 7607 |
| **Nov** | 5418 | 5418 | 592 | 102 | 6112 |
| **Dec** | 7153 | 7153 | 815 | 136 | 8104 |
| **Y.T.D.** | **81,030** | **81,030 (89.33%)** | **7,877 (8.68%)** | **1,806 (1.99%)** | **90,713** |

## Appendix 3: Newborn Screening Laboratory Report – Abnormal Results 2008

| Disorder | | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | Y.T.D. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| BIO* | Confirmed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | Referred | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| CAH | Confirmed | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | **5** |
| | High Risk | 6 | 14 | 10 | 12 | 6 | 5 | 16 | 7 | 3 | 12 | 5 | 11 | **107** |
| | Borderline Risk | 19 | 23 | 27 | 21 | 38 | 26 | 31 | 17 | 27 | 19 | 25 | 47 | **320** |
| CF | Confirmed | 3 | 1 | 2 | 1 | 2 | 1 | 5 | 2 | 1 | 2 | 1 | 4 | **25** |
| | Referred | 10 | 8 | 9 | 7 | 7 | 15 | 11 | 10 | 4 | 7 | 2 | 12 | **102** |
| CH | Confirmed | 3 | 3 | 2 | 3 | 1 | 4 | 2 | 1 | 4 | 5 | 4 | 3 | **35** |
| | High Risk | 6 | 5 | 7 | 7 | 3 | 6 | 4 | 3 | 4 | 9 | 7 | 3 | **64** |
| | Borderline Risk | 66 | 66 | 59 | 53 | 59 | 52 | 44 | 40 | 55 | 63 | 50 | 76 | **683** |
| GAL | Confirmed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | High Risk | 1 | 1 | 0 | 0 | 4 | 3 | 5 | 8 | 1 | 2 | 0 | 3 | **28** |
| | Borderline Risk | 2 | 6 | 1 | 8 | 6 | 13 | 26 | 6 | 13 | 6 | 2 | 18 | **107** |
| AA | Confirmed | 1 | 1 | 1 | 0 | 3 | 0 | 2 | 0 | 0 | 1 | 0 | 1 | **10** |
| | High Risk | 2 | 1 | 2 | 0 | 2 | 0 | 2 | 0 | 1 | 1 | 0 | 2 | **13** |
| | Moderate Risk | 5 | 0 | 0 | 2 | 3 | 0 | 2 | 1 | 1 | 2 | 5 | 0 | **21** |
| | Low Risk | 59 | 48 | 44 | 87 | 33 | 22 | 22 | 22 | 34 | 33 | 40 | 81 | **525** |
| OA | Confirmed | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 2 | 1 | 1 | 1 | 1 | **10** |
| | High Risk | 2 | 0 | 1 | 1 | 0 | 0 | 0 | 3 | 0 | 1 | 1 | 1 | **10** |
| | Moderate Risk | 2 | 2 | 0 | 0 | 1 | 2 | 2 | 0 | 1 | 1 | 0 | 0 | **11** |
| | Low Risk | 22 | 20 | 24 | 26 | 11 | 22 | 26 | 19 | 25 | 32 | 30 | 39 | **296** |
| FA | Confirmed | 2 | 0 | 5 | 1 | 0 | 2 | 1 | 2 | 1 | 2 | 4 | 1 | **21** |
| | High Risk | 2 | 0 | 3 | 1 | 0 | 11 | 0 | 0 | 3 | 4 | 1 | 1 | **16** |
| | Moderate Risk | 2 | 0 | 4 | 0 | 1 | 1 | 0 | 5 | 3 | 4 | 2 | 0 | **22** |
| | Low Risk | 30 | 30 | 27 | 42 | 20 | 42 | 29 | 31 | 43 | 25 | 20 | 28 | **367** |

*continued*

| Disorder | | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | Y.T.D. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hb* | Sickle Cell Disease | 4 | 0 | 4 | 7 | 7 | 4 | 1 | 2 | 3 | 1 | 2 | 1 | **36** |
| | Other Hemoglobinopathies | 1 | 0 | 0 | 1 | 1 | 2 | 1 | 2 | 0 | 0 | 0 | 0 | **8** |
| | Abnormal Traits | 152 | 136 | 130 | 163 | 124 | 125 | 132 | 162 | 136 | 128 | 107 | 155 | **1650** |
| | | | | | | | | | | | | Total Confirmed | | **150** |

*BIO = biotinidase deficiency; started screening Dec. 2008

CAH = congenital adrenal hyperplasia CH = congenital hypothyroidism AA = amino acid FA = fatty acid

CF = cystic fibrosis GAL = galactosemia OA = organic acid Hb = hemoglobinopathies

*See Appendix 5 for further hemoglobinopathy results.

Average laboratory turnaround times from receipt of specimen to reporting are:

| Results | Turnaround Times |
|---|---|
| High Risk Result* | 1.5 days |
| Low/Borderline Risk** | 4 - 6 days |
| Normal Result ** | 4 - 6 days |

* the result is telephoned and faxed to the physician of record

** hard copy reports are mailed to the physician of record and the submitting facility; final abnormal results are also included in this category

## Outcome Data - Newborn Screening Specimens and Results

- In 2008 there were 81,030 babies tested in the state newborn screening laboratory. There were 90,713 blood spot specimens received in the laboratory. Specimens received included:

| Initial | Repeat | Unsatisfactory |
|---|---|---|
| 81,030 | 7,877 | 1,806 |

- In the process of screening newborns for 66 genetic and metabolic conditions, it is the newborn screening laboratory's role to assess the risk of any abnormal screening results by evaluating the marker analytes present and the levels that were detected. This risk assessment then dictates different levels of action and follow up protocols. The three categories of risk and the number of test results falling in these categories during 2008 were:

| High Risk | Moderate Risk | Low / Borderline Risk |
|---|---|---|
| 360 (0.44%) | 54 (0.07%) | 2,298 (2.8%) |

**High Risk -** Results are immediately phoned and faxed to the physician of record and to the contracted genetic referral centers for consultation and confirmatory testing. Final laboratory reports are mailed to the facility that submitted the specimen and the physician of record.

**Moderate Risk** - Results are immediately phoned and faxed to the physician of record and to the contracted genetic referral centers for consultation and confirmatory testing. Final laboratory reports are mailed to the facility that submitted the specimen and the physician of record.

**Low / Borderline Risk –** Final laboratory results are mailed to the physician of record and submitting facility and a repeat newborn screen is necessary.

- One hundred fifty (150) confirmed disorders were diagnosed from these abnormal newborn screening results during 2008.

## Appendix 4: 2008 Unsatisfactory Samples

| | |
|---|---|
| **LAYERED CLOTTED OR SUPERSATURATED:** Possible causes: Touching the same circle on filter paper to blood drop several times; filling circle on both sides of filter paper; application of excess blood; clotted swirl marks from improper capillary application. Use of unheparinized capillary tube. | 492 |
| **INCOMPLETE SATURATION:** Uneven saturation; blood did not soak through the filter paper. Possible causes: Removing filter paper before blood has completely filled circle or before blood has soaked through to opposite side; improper capillary tube application; allowing filter paper to come in contact with gloved or ungloved hands or substances such as hand lotion or powder, either before or after blood specimen collection. | 373 |
| **DILUTED, DISCOLORED OR CONTAMINATED:** Possible causes: squeezing or milking of area surrounding the puncture site; allowing filter paper to come in contact with gloved or ungloved hands, or substances such as alcohol, formula, antiseptic solutions, water, hand lotion, powder, etc., either before or after blood specimen collection; exposing blood spots to direct heat; allowing blood spots to come in contact with tabletop, etc. while drying the sample. | 372 |
| **BLOOD ON OVERLAY COVER:** Overlay cover came in contact with wet blood specimen. Sample is unsatisfactory for testing because blood soaked from back of filter onto the gold colored backing of the form. The filter circles are designed to hold a specific quantity of blood. If the wet filter is allowed to come in contact with the paper backing of form, blood can be drawn out of filter making the quantitative tests performed by the Newborn Screening Laboratory invalid. Allow blood spots to thoroughly air dry for at least 2 hours in a horizontal position, away from direct heat and sunlight. Do not allow the blood to touch any surface during drying, including other parts of the form. | 238 |
| **SPECIMEN ABRADED:** Filter scratched, torn or abraded. Possible causes: Improper use of capillary tubes. To avoid damaging the filter paper fibers, do not allow the capillary tube to touch the filter paper. Actions such as "coloring in" the circle, repeated dabbing around the circle, or any technique that may scratch, compress, or indent the paper should not be used. | 137 |
| **QUANTITY NOT SUFFICIENT:** Quantity of blood on filter not sufficient for testing. Possible causes: Removing filter paper before blood has completely filled circle; not allowing an ample sized blood drop to form before applying to filter; inadequate heel stick procedure. | 112 |
| **OLD SPECIMEN:** Specimen greater than 15 days old when received at State Public Health Laboratory. The collection card should be transported or mailed to the Newborn Screening Laboratory within 24 hours after specimen collection. Avoid the practice of holding onto specimens to wait for more to accumulate before mailing, also referred to as "batching" the specimens. Although batching may seem more efficient, it's not worth it in the long run because a delay in screening and treatment can cause irreparable damage to a child with metabolic disease. | 50 |
| **OLD FORM:** Sample received on out-of-date form. Samples received on outdated Newborn Screening cards will not be accepted. Please contact Missouri Department of Health and Senior Services, Newborn Screening Unit at (573) 751-2662 to obtain updated screening forms. | 8 |
| **SERUM RINGS:** Serum separated into clear rings around blood spot. Possible causes: Card dried vertically (on side) instead of flat; squeezing excessively around puncture site; allowing filter paper to come in contact with alcohol, hand lotion, etc. | 8 |
| **MISSING OR INCOMPLETE PATIENT INFORMATION:** Missing or incomplete demographic information. | 5 |
| **NO BLOOD:** Filter submitted without blood. | 5 |
| **WET SPECIMEN:** Specimen submitted before drying thoroughly. Allow blood spots to thoroughly dry for at least 3 hours in a horizontal position, away from direct heat and sunlight. Do not allow the blood to touch any surface during drying, including other parts of the card. | 3 |
| **OTHER UNSUITABLE** | 2 |
| **FILTER AND FORM BARCODES DO NOT MATCH:** Bar code on filter does not match bar code on Newborn Screening Form. Collection forms contain barcodes on demographic, hearing and filter portions. The barcodes may not be altered in any way. If incorrect baby is sampled do not remove filter and attach to a different demographic portion. If a sampling error occurs the entire form needs to be voided and sample needs to be recollected on a new form. All barcodes must match laboratory copy, submitter copy, newborn hearing screen, and filter. | 1 |
| **Total Unsatisfactory Specimens Received** | 1,806 (2%) |

## Appendix 5: Hemoglobinopathy Report 2008

Specimens Received:

| | | |
|---|---|---|
| Initial: | 81,030 | (89.1%) |
| Repeat: | 7,877 | (8.7%) |
| Unsatisfactory: | 1,806 | (2.0%) |
| Whole Blood: | 200 | (0.2%) |
| **Total:** | **90,913** | |

| Analyses (Tests) Performed: | IEF | HPLC | Total |
|---|---|---|---|
| First Tests: | 90,706 (83.1%) | - | 90,706 (78.1%) |
| Retests: | 3,255 (3.0%) | 3,860 (55.0%) | 7,115 (6.1%) |
| Controls/Standards: | 14,897 (13.6%) | 2,893 (41.2%) | 17,790 (15.3%) |
| Proficiency Testing: | 68 (.1%) | 45 (.6%) | 113 (.1%) |
| Whole Blood Tests: | 242 (.2%) | 224 (3.2%) | 466 (.4%) |
| **Total:** | **109,168** | **7,022** | **116,190** |

| **Significant Screening Results = 1,694** | | | | | |
|---|---|---|---|---|---|
| **Sickle Cell Disease*** | | **Other Disease Conditions*** | | **Trait Conditions** | |
| FS | 20 | FC | 3 | FAS | 978 |
| FSC | 11 | FCX | 1 | FAC | 292 |
| FSA | 3 | FDA | 1 | FAX | 38 |
| FSX | 2 | Highly Elevated Barts | 2 | FAE | 49 |
| | | FCE | 1 | FAD | 36 |
| | | | | FASX | 2 |
| | | | | Slightly Elevated Barts | 10 |
| | | | | FAG | 2 |
| | | | | FSAINC | 106 |
| | | | | FCAINC | 37 |
| **Total** | **36* (2.1%)** | **Total** | **8* (.5%)** | **Total** | **1,650 (97.4%)** |

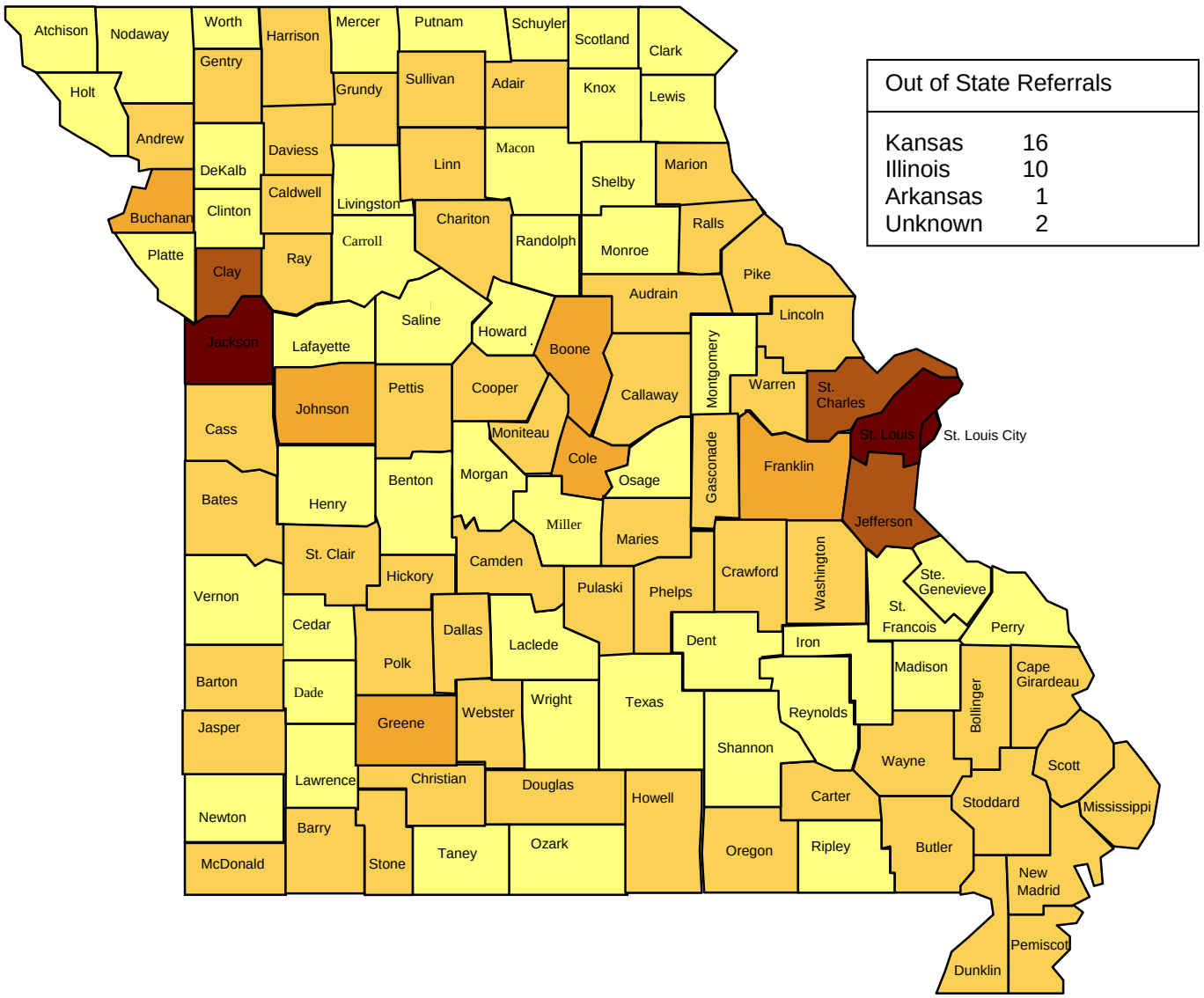
* These are screening results and not confirmed. Total of 44 possible disease conditions detected at screening.

| **Geographic Follow-up of Significant Disease and Trait Conditions** | | | | | |
|---|---|---|---|---|---|
| **Significant Disease Conditions** | | | **"S" Trait Conditions Only (includes repeats)** | | |
| St. Louis Area | 27 | 61% | St. Louis Area | 662 | 59% |
| Kansas City Area | 9 | 21% | Kansas City Area | 266 | 24% |
| Remainder of MO | 8 | 18% | Remainder of MO | 196 | 17% |
| **Total** | **44**** | **100%** | **Total** | **1124** | **100%** |

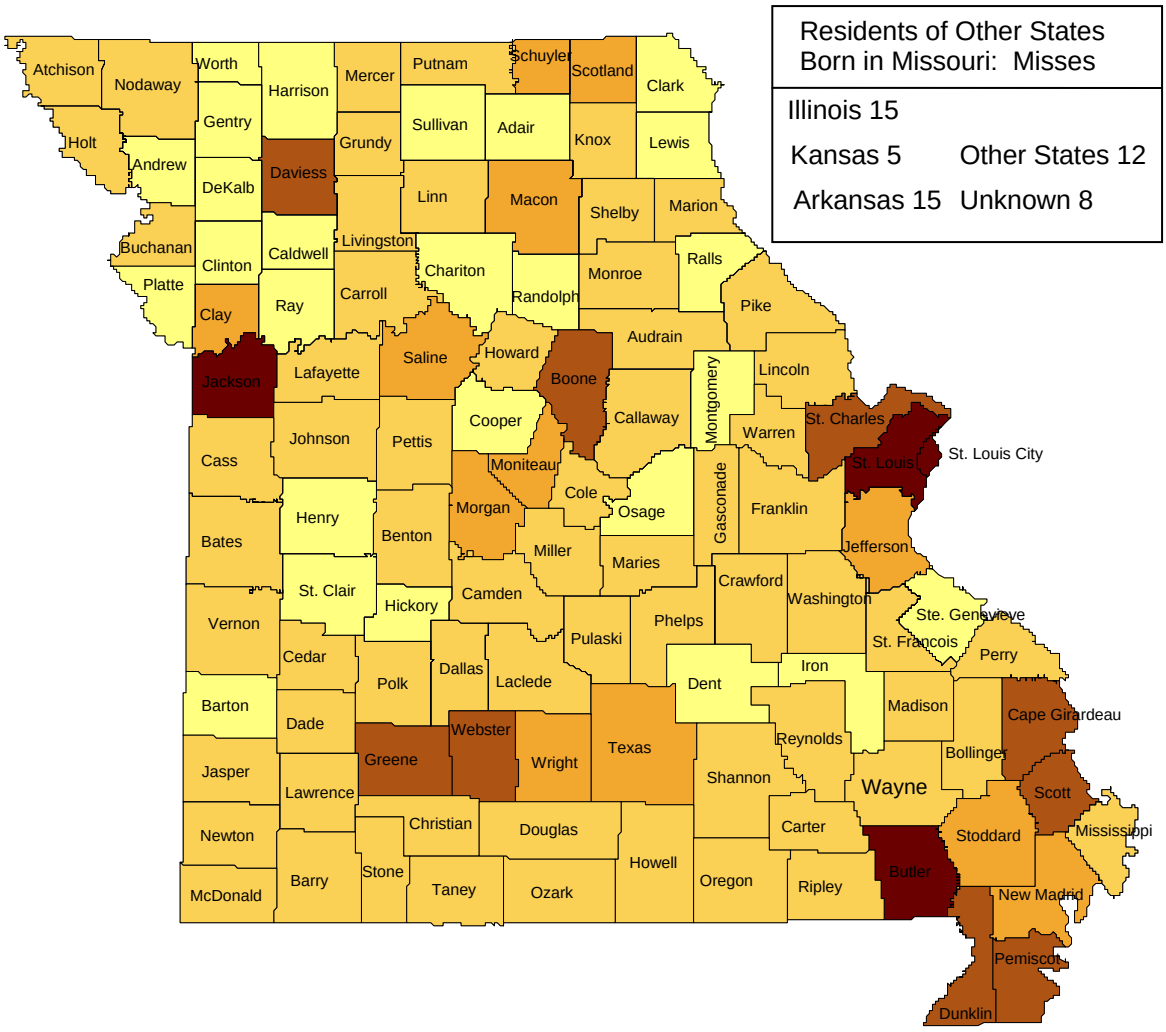
** Of the 44 significant conditions found at screening, 39 were confirmed as disease conditions. See Appendix 1.

Note: Because of rounding, percentages will not necessarily add to exactly 100%.

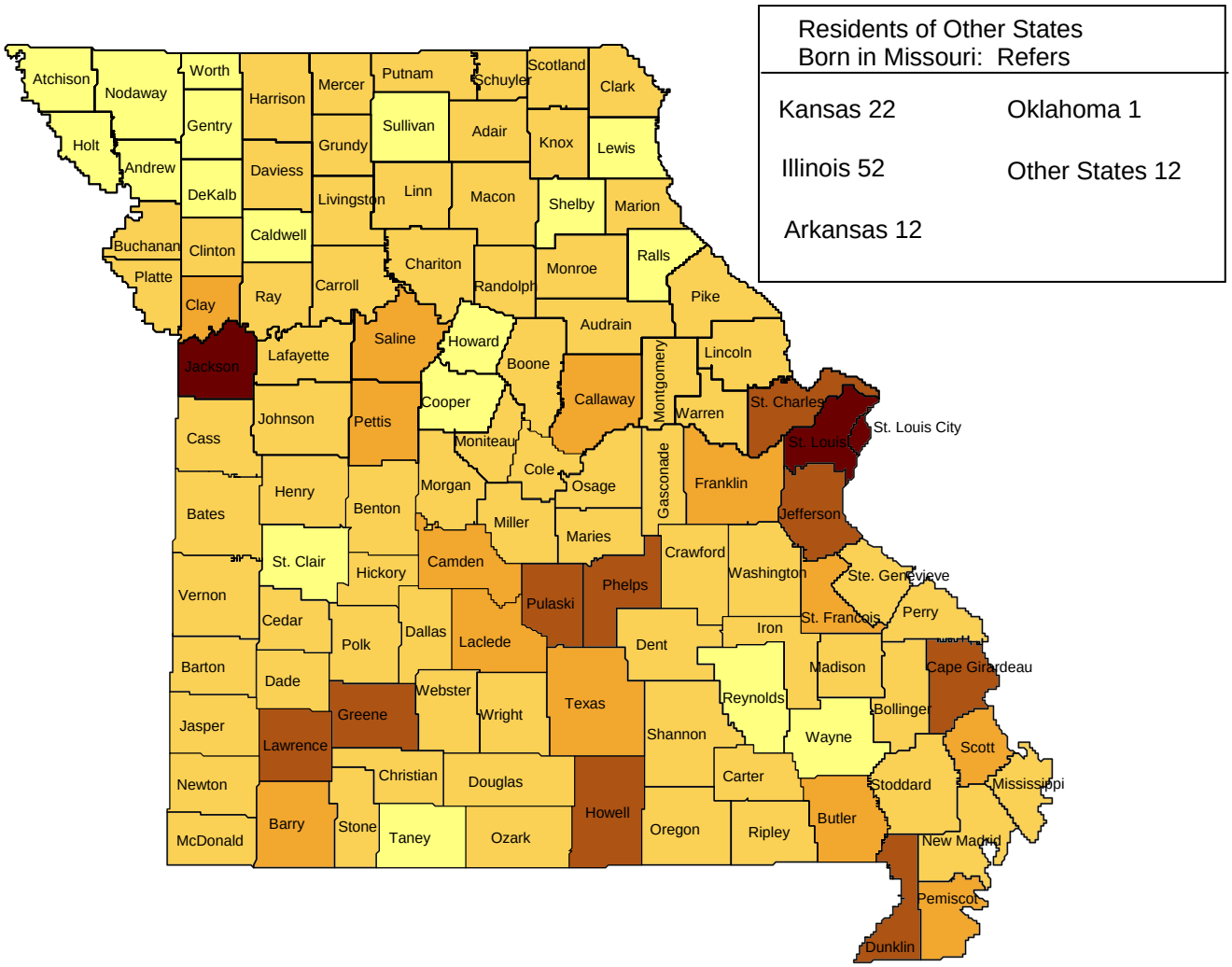
# Appendix 6: 2008 Referrals from Missouri Newborn Bloodspot Screening Program



# Appendix 7: 2008 Misses from Missouri Newborn Hearing Screening



# Appendix 8: 2008 Refers from Missouri Newborn Hearing Screening



## Appendix 9: Newborn Screening Satisfaction Surveys

A satisfaction survey of parents and physicians was conducted for families of babies having abnormal newborn screening results reported in 2006. Key findings:

| Newborn Screening Parent Satisfaction Survey - Parent Response | | | | |
|---|---|---|---|---|
| | Very Satisfied | Satisfied | Not Satisfied | No Response |
| Explanation of abnormal MS/MS results | 33% | 40% | 27% | 0% |
| Timeliness on notification of abnormal MS/MS screen results | 47% | 40% | 7% | 6% |
| Number of follow-up tests or newborn screen results done to determine diagnosis | 20% | 60% | 13% | 7% |
| Timeliness of follow-up tests and/or newborn screen | 27% | 40% | 20% | 13% |
| Answers to parents' questions about the disorders screened and testing methodology | 33% | 40% | 27% | 0% |

Reasons cited for "not satisfied" in the above parent survey were:

1. Didn't like the genetic counselor.
2. Physicians not knowledgeable on the screened diseases, making a difficult situation worse.
3. Educate doctors, nurses, ERs as they lack the knowledge and are the first line of defense.
4. Need handouts to explain results and what they mean, and the chance that the results are incorrect.
5. Didn't like to have to pay extra to have baby retested; tested during pilot and was told it is likely to have a false positive. Not given a good explanation about what the problem could be.
6. Wanted survey in Spanish.
7. Need an information sheet on item that was wrong.
8. Why didn't they start screening sooner?
9. Concerned because I didn't know what disorders were included on test, with a brief explanation.
10. Too much blood was taken.

| Newborn Screening Physician Satisfaction | | | |
|---|---|---|---|
| | Very Satisfied | Satisfied | Not Satisfied |
| Timeliness on notification of abnormal MS/MS newborn results | 79% | 21% | 0% |
| Method of receiving abnormal MS/MS results | 82% | 14% | 4% |
| Information contained in the newborn screen report | 87% | 11% | 2% |

| | | | |
|---|---|---|---|
| Result interpretation of newborn screen report | 79% | 18% | 3% |
| Ease on contacting a genetic tertiary center for consultation | 79% | 18% | 3% |
| Recommendations of the genetic tertiary center | 82% | 11% | 7% |

Reasons cited for "not satisfied" in the above physician survey were:

1. The information provided is not enough – too generic.
2. Wanted phone call from the state lab.
3. Had to call specialty center for information.

A satisfaction survey of parents of infants and children receiving services provided by the hemoglobinopathy resource centers was completed in 2007. Key findings:

| **Hemoglobinopathy Resource Center Satisfaction Survey - Parent Response** | | | |
|---|---|---|---|
| | Very Satisfied | Satisfied | Not Satisfied |
| Treated with respect | 88% | 12% | 0% |
| Treatment staff was knowledgeable | 86% | 14% | 0% |
| Questions/concerns addressed in a timely manner | 83% | 17% | 0% |
| Staff provided useful referrals and resources | 81% | 19% | 0% |
| Provided with the services needed | 83% | 17% | 0% |
| Medical care/services received | 78% | 22% | 0% |
| Received services or treatment without experiencing any problems | 99% | 0% | 1% |

Only one response was given for "not satisfied" in the above parent survey: "*Nursing staff and doctors are not nice, sometimes talking to you as if you don't know what you are speaking of.*"

## Appendix 10: Newborn Hearing Screening Survey

A satisfaction survey of parents of children born in 2006 who went through the newborn hearing screening and audiologic assessment process was completed in June 2007.

Key findings:

- 89% of respondents were very satisfied or satisfied with the newborn hearing screening process.
- 7% of respondents were somewhat satisfied.
- 4% of respondents were not satisfied.

In addition:

- 95% of the respondents reported that the birth hospital notified them of the screening result.
- 86% of the respondents reported that the birth hospital provided them with the newborn hearing screening program brochure.

Reasons cited for “not satisfied” in the survey were:

- Cost of the rescreen/diagnostic evaluation – five comments.
- Pediatrician handled rescreen or referral to audiologist poorly – two comments.
- Hospital issues such as poor communication with parent or physician and lack of interest in hearing screening – three comments.
- Hospital rescreened numerous times in order to get a “pass” result – one comment.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